

IN THE CLAIMS

Please amend the claims as follows:

Claims 1-17 (Canceled).

Claim 18 (Currently Amended): An isolated polynucleotide encoding a protein that suppresses or promotes the aggregation or deposition of amyloid- $\beta$  protein, wherein the polynucleotide is selected from the group consisting of:

(a) a polynucleotide that comprises a nucleotide sequence as set forth in SEQ ID NO: 1, 3, 5, 7 or 9,

(b) a polynucleotide that encodes a protein having an amino acid sequence as set forth in SEQ ID NO: 2, 4, 6, 8 or 10,

(c) a polynucleotide that encodes a protein ~~functionally equivalent to the protein of (b) comprising an amino acid sequence~~ in which one or several amino acids of the amino acid sequence of SEQ ID NO: 2, 4, 6, 8 or 10, have been substituted, deleted, inserted and/or added, wherein the overall percentage of mutations is ~~typically 10%~~ 5% or less,

(d) a polynucleotide that hybridizes under stringent conditions to a polynucleotide comprising a nucleotide sequence as set forth in SEQ ID NO: 1, 3, 5, 7 or 9, wherein the stringent conditions comprise washing in 0.1 X SSC and 0.1% SDS at 65°C; or, and

(e) a polynucleotide that shows at least (i) ~~60%~~, (ii) ~~70%~~, (iii) ~~80%~~, (iv) ~~90%~~, or (v) 95% homology identity to a nucleotide sequence as set forth in SEQ ID NO: 1, 3, 5, 7 or 9.

Claim 19 (Withdrawn): A protein encoded by a polynucleotide according to Claim 18.

Claim 20 (Withdrawn): A protein that suppresses or promotes the aggregation of amyloid- $\beta$  protein, wherein said protein is encoded by a polynucleotide that, from a molecular evolutionary aspect, originated from the same gene from which a polynucleotide according to Claim 1 originated from.

Claim 21 (Previously Presented): A vector comprising a polynucleotide according to Claim 18.

Claim 22 (Previously Presented): A transfectant harboring a polynucleotide according to Claim 18.

Claim 23 (Previously Presented): A transfectant harboring the vector according to Claim 21.

Claim 24 (Currently Amended): A method for producing the a protein that suppresses or promotes the aggregation or deposition of amyloid- $\beta$  protein according to Claim 19, wherein said method comprises the steps of culturing the transfectant harboring a the polynucleotide according to Claim 18 ~~encoding a protein that suppresses or promotes the aggregation or deposition of amyloid- $\beta$  protein, wherein the polynucleotide is selected from the group consisting of:~~

~~(a) a polynucleotide that comprises a nucleotide sequence as set forth in SEQ ID NO: 1, 3, 5, 7 or 9,~~

~~(b) a polynucleotide that encodes a protein having a amino acid sequence as set forth in SEQ ID NO: 2, 4, 6, 8 or 10,~~

~~(c) a polynucleotide that encodes a protein functionally equivalent to the protein of (b) comprising an amino acid sequence in which one or several amino acids of the amino acid sequence of SEQ ID NO. 2, 4, 6, 8 or 10, have been substituted, deleted, inserted and/or added, wherein the overall percentage of mutations is typically 10% or less.~~

~~(d) a polynucleotide that hybridizes under stringent conditions to a polynucleotide comprising a nucleotide sequence as set forth in SEQ ID NO. 1, 3, 5, 7 or 9; or,~~

~~(e) a polynucleotide that shows at least (i) 60%, (ii) 70%, (iii) 80%, (iv) 90%, or (v) 95% homology to a nucleotide sequence as set forth in SEQ ID NO. 1, 3, 5, 7 or 9, and recovering the expression product.~~

Claim 25 (Currently Amended): A method for producing the a protein that suppresses or promotes the aggregation or deposition of amyloid- $\beta$  protein according to Claim 19, wherein said method comprises: the steps of

culturing the transfectant harboring the vector according to Claim 21 comprising a polynucleotide encoding a protein that suppresses or promotes the aggregation or deposition of amyloid- $\beta$  protein, wherein the polynucleotide is selected from the group consisting of:

~~(a) a polynucleotide that comprises a nucleotide sequence as set forth in SEQ ID NO. 1, 3, 5, 7 or 9,~~

~~(b) a polynucleotide that encodes a protein having a amino acid sequence as set forth in SEQ ID NO. 2, 4, 6, 8 or 10,~~

~~(c) a polynucleotide that encodes a protein functionally equivalent to the protein of (b) comprising an amino acid sequence in which one or several amino acids of the amino acid sequence of SEQ ID NO. 2, 4, 6, 8 or 10, have been substituted, deleted, inserted and/or added, wherein the overall percentage of mutations is typically 10% or less.~~

~~(d) a polynucleotide that hybridizes under stringent conditions to a polynucleotide comprising a nucleotide sequence as set forth in SEQ ID NO. 1, 3, 5, 7 or 9; or,~~

~~(e) a polynucleotide that shows at least (i) 60%, (ii) 70%, (iii) 80%, (iv) 90%, or (v) 95% homology to a nucleotide sequence as set forth in SEQ ID NO. 1, 3, 5, 7 or 9, and recovering the expression product.~~

Claim 26 (Withdrawn): An antibody against the protein according to Claim 19.

Claim 27 (Withdrawn, Currently Amended): An immunological assay comprising:  
~~the step of~~

monitoring an immunological reaction between the protein according to Claim 19 and the antibody against the protein encoded by a polynucleotide encoding a protein that suppresses or promotes the aggregation or deposition of amyloid- $\beta$  protein, wherein the polynucleotide is selected from the group consisting of:

(a) a polynucleotide that comprises a nucleotide sequence as set forth in SEQ ID NO: 1, 3, 5, 7 or 9,

(b) a polynucleotide that encodes a protein having a amino acid sequence as set forth in SEQ ID NO: 2, 4, 6, 8 or 10,

(c) a polynucleotide that encodes a protein functionally equivalent to the protein of (b) comprising an amino acid sequence in which one or several amino acids of the amino acid sequence of SEQ ID NO: 2, 4, 6, 8 or 10, have been substituted, deleted, inserted and/or added, wherein the overall percentage of mutations is ~~typically 10%~~ 5% or less.

(d) a polynucleotide that hybridizes under stringent conditions to a polynucleotide comprising a nucleotide sequence as set forth in SEQ ID NO: ~~1, 3, 5, 7 or 9; or,~~ and

(e) a polynucleotide that shows at least (i) 60%, (ii) 70%, (iii) 80%, (iv) 90%, or (v) 95% ~~homology~~ identity to a nucleotide sequence as set forth in SEQ ID NO<sub>1</sub>, 3, 5, 7 or 9.

Claim 28 (Withdrawn, Currently Amended): A method of screening for a compound that regulates the activity of a protein encoded by a polynucleotide according to Claim 18, ~~wherein said method comprises the following steps of~~ comprising:

(a) contacting a candidate compound with said protein, or with a cell expressing said protein, in the presence of amyloid- $\beta$  protein, and,

(b) selecting a the candidate compound that regulates the aggregation or deposition of amyloid- $\beta$  protein.

Claim 29 (Withdrawn, Currently Amended): A method of screening for a compound that regulates expression of a protein encoded by a polynucleotide according to Claim 18, ~~wherein said method comprises the following steps~~ comprising:

(a) contacting a candidate compound with a cell, wherein a vector has been introduced into said cell, said vector comprising:

(i) an expression regulatory region of a gene comprising a nucleotide sequence selected from the group consisting of ~~SEQ ID NO. 1~~, SEQ ID NO<sub>1</sub>, 3, SEQ ID NO<sub>1</sub>, 5, SEQ ID NO<sub>1</sub>, 7, and SEQ ID NO<sub>1</sub>, 9, and,

(ii) a reporter gene operably linked downstream of the expression regulatory region,

(b) measuring the presence of the reporter gene, and,

(c) selecting the candidate compound that increases or decreases the reporter activity measured in step (b) when compared to the control.

Claim 30 (Withdrawn): A pharmaceutical agent comprising a compound obtained by the method according to Claim 28.

Claim 31 (Withdrawn): A pharmaceutical agent comprising the protein according to Claim 19.

Claim 32 (Withdrawn): A pharmaceutical agent comprising the protein according to Claim 20.

Claim 33 (Withdrawn): A pharmaceutical agent comprising an antisense polynucleotide complementary to the protein-coding sequence of a polynucleotide according to Claim 18.

Claim 34 (Withdrawn, Currently Amended): A pharmaceutical agent for ~~prevention~~ preventing or treating of Alzheimer's disease, wherein said pharmaceutical agent comprising a compound obtained by the method according to Claim 28.

Claim 35 (Withdrawn, Currently Amended): A method for detecting Alzheimer's disease, comprising ~~the following steps of:~~

- (a) measuring the expression of a polynucleotide according to Claim 18,
- (b) comparing the measurement obtained in (a) with that obtained when the polynucleotide is expressed in healthy subjects and detecting a change in expression, and
- (c) linking Alzheimer's disease with said change in expression of the polynucleotide.

Claim 36 (Withdrawn, Currently Amended): A method for preventing or treating Alzheimer's disease, ~~wherein the method comprises~~ comprising:

administering a pharmaceutical composition comprising as an active ingredient a compound obtained by the method according to Claim 28.

Claim 37 (Currently Amended): An isolated polynucleotide encoding a ~~partial peptide of a protein encoded by a polynucleotide encoding~~ a protein that suppresses or promotes the aggregation or deposition of amyloid- $\beta$  protein, wherein the protein is encoded by a polynucleotide is selected from the group consisting of:

(a) a polynucleotide that comprises a nucleotide sequence as set forth in SEQ ID NO: ~~1~~, 3, 5, 7 or 9,

(b) a polynucleotide that encodes a protein having a amino acid sequence as set forth in SEQ ID NO: 2, 4, 6, 8 or 10,

(c) a polynucleotide that encodes a protein ~~functionally equivalent to the protein of (b) comprising an amino acid sequence~~ in which one or several amino acids of the amino acid sequence of SEQ ID NO: ~~2~~, 4, 6, 8 or 10, have been substituted, deleted, inserted and/or added, wherein the overall percentage of mutations is ~~typically 10%~~ 5% or less,

(d) a polynucleotide that hybridizes under stringent conditions to a polynucleotide comprising a nucleotide sequence as set forth in SEQ ID NO: ~~1~~, 3, 5, 7 or 9, wherein the stringent conditions comprise washing in 0.1 X SSC and 0.1% SDS at 65°C; or, and

(e) a polynucleotide that shows at least ~~(i) 60%, (ii) 70%, (iii) 80%, (iv) 90%, or (v)~~ 95% homology identity to a nucleotide sequence as set forth in SEQ ID NO: ~~1~~, 3, 5, 7 or 9, wherein said partial peptide (a) suppresses or promotes amyloid- $\beta$  protein aggregation, or (b) raises is used to provide a specific antibody against the whole protein by immunization.

Claim 38 (Withdrawn): A peptide encoded by the polynucleotide according to Claim 37.

Claim 39 (Previously Presented): A vector comprising the polynucleotide according to Claim 37.

Claim 40 (Previously Presented): A transfectant harboring the polynucleotide according to Claim 37.

Claim 41 (Previously Presented): A transfectant harboring the vector according to Claim 39.

Claim 42 (Currently Amended): A method for producing a partial peptide of a protein that suppresses or promotes the aggregation or deposition of amyloid- $\beta$  protein ~~the peptide~~ Claim 38, wherein said method comprises: ~~the steps of~~

culturing the transfectant harboring the polynucleotide according to Claim 37 ~~encoding a partial peptide of a protein encoded by a polynucleotide encoding a protein that suppresses or promotes the aggregation or deposition of amyloid- $\beta$  protein, wherein the polynucleotide is selected from the group consisting of:~~

(a) ~~a polynucleotide that comprises a nucleotide sequence as set forth in SEQ ID NO: 1, 3, 5, 7 or 9,~~

(b) ~~a polynucleotide that encodes a protein having a amino acid sequence as set forth in SEQ ID NO: 2, 4, 6, 8 or 10,~~

(c) ~~a polynucleotide that encodes a protein functionally equivalent to the protein of (b) comprising an amino acid sequence in which one or several amino acids of the amino acid~~



~~sequence of SEQ ID NO. 2, 4, 6, 8 or 10, have been substituted, deleted, inserted and/or added, wherein the overall percentage of mutations is typically 10% or less.~~

~~(d) a polynucleotide that hybridizes under stringent conditions to a polynucleotide comprising a nucleotide sequence as set forth in SEQ ID NO. 1, 3, 5, 7 or 9; or,~~

~~(e) a polynucleotide that shows at least (i) 60%, (ii) 70%, (iii) 80%, (iv) 90%, or (v) 95% homology to a nucleotide sequence as set forth in SEQ ID NO. 1, 3, 5, 7 or 9, wherein said partial peptide (a) suppresses or promotes amyloid- $\beta$  protein aggregation, or (b) is used to provide a specific antibody against the whole protein; and~~

~~recovering the expression product.~~

Claim 43 (Currently Amended): A method for producing a partial peptide of a protein that suppresses or promotes the aggregation or deposition of amyloid- $\beta$  protein the peptide Claim 38, wherein said method comprises: ~~the steps of~~

~~culturing the transfectant harboring the vector according to Claim 39 comprising the polynucleotide encoding a partial peptide of a protein encoded by a polynucleotide encoding a protein that suppresses or promotes the aggregation or deposition of amyloid- $\beta$  protein; wherein the polynucleotide is selected from the group consisting of:~~

~~(a) a polynucleotide that comprises a nucleotide sequence as set forth in SEQ ID NO: 1, 3, 5, 7 or 9;~~

~~(b) a polynucleotide that encodes a protein having a amino acid sequence as set forth in SEQ ID NO: 2, 4, 6, 8 or 10;~~

~~(c) a polynucleotide that encodes a protein functionally equivalent to the protein of (b) comprising an amino acid sequence in which one or several amino acids of the amino acid sequence of SEQ ID NO. 2, 4, 6, 8 or 10, have been substituted, deleted, inserted and/or added, wherein the overall percentage of mutations is typically 10% or less.~~

~~(d) a polynucleotide that hybridizes under stringent conditions to a polynucleotide comprising a nucleotide sequence as set forth in SEQ ID NO. 1, 3, 5, 7 or 9; or,~~

~~(e) a polynucleotide that shows at least (i) 60%, (ii) 70%, (iii) 80%, (iv) 90%, or (v) 95% homology to a nucleotide sequence as set forth in SEQ ID NO. 1, 3, 5, 7 or 9, wherein said partial peptide (a) suppresses or promotes amyloid- $\beta$  protein aggregation, or (b) is used to provide a specific antibody against the whole protein, and~~

recovering the expression product.

Claim 44 (Withdrawn): An antibody against the peptide according to Claim 38.

Claim 45 (Currently Amended): An immunological assay comprising: ~~the step of:~~  
monitoring an immunological reaction between the peptide according to Claim 38 and the antibody against the peptide encoded by the polynucleotide encoding a partial peptide of a protein encoded by a polynucleotide encoding a protein that suppresses or promotes the aggregation or deposition of amyloid- $\beta$  protein, wherein the polynucleotide is selected from the group consisting of:

(a) a polynucleotide that comprises a nucleotide sequence as set forth in SEQ ID NO: 1, 3, 5, 7 or 9,

(b) a polynucleotide that encodes a protein having a amino acid sequence as set forth in SEQ ID NO: 2, 4, 6, 8 or 10,

(c) a polynucleotide that encodes a protein functionally equivalent to the protein of (b) comprising an amino acid sequence in which one or several amino acids of the amino acid sequence of SEQ ID NO: 2, 4, 6, 8 or 10, have been substituted, deleted, inserted and/or added, wherein the overall percentage of mutations is ~~typically 10%~~ 5% or less.

(d) a polynucleotide that hybridizes under stringent conditions to a polynucleotide comprising a nucleotide sequence as set forth in SEQ ID NO. 1, 3, 5, 7 or 9; ~~or, and~~

(e) a polynucleotide that shows at least (i) 60%, (ii) 70%, (iii) 80%, (iv) 90%, or (v) 95% ~~homology~~ identity to a nucleotide sequence as set forth in SEQ ID NO. 1, 3, 5, 7 or 9, wherein said partial peptide (a) suppresses or promotes amyloid- $\beta$  protein aggregation, or (b) is used to provide a specific antibody against the whole protein.

Claim 46 (Currently Amended): A method of screening for a compound that regulates the activity of a peptide encoded by the polynucleotide according to Claim 37, ~~wherein, said method comprises the following steps of~~ comprising:

(a) contacting a candidate compound with said protein, or with a cell expressing said protein, in the presence of amyloid- $\beta$  protein, and;

(b) selecting a the candidate compound that regulates the aggregation or deposition of amyloid- $\beta$  protein.

Claim 47 (Currently Amended): A method of screening for a compound that regulates expression of a peptide encoded by a polynucleotide according to Claim 37, comprising; ~~wherein said method comprises the following steps of~~:

(a) contacting a candidate compound with a cell, wherein a vector has been introduced into said cell, said vector comprising:

(i) an expression regulatory region of a gene comprising a nucleotide sequence selected from the group consisting of ~~SEQ ID NO. 1~~, SEQ ID NO. 3, SEQ ID NO. 5, SEQ ID NO. 7, and SEQ ID NO. 9, and,

(ii) a reporter gene operably linked downstream of the expression regulatory region,

- (b) measuring the presence of the reporter gene, and,
- (c) selecting the candidate compound that increases or decreases the reporter activity measured in step (b) when compared to the control.

Claim 48 (Previously Presented): A pharmaceutical agent comprising a compound obtained by the method according to Claim 46.

Claim 49 (Previously Presented): A pharmaceutical agent comprising the peptide according to Claim 38.

Claim 50 (Previously Presented): A pharmaceutical agent comprising an antisense polynucleotide complementary to the protein-coding sequence of the polynucleotide according to Claim 37.

Claim 51 (Currently Amended): A pharmaceutical agent for prevention or treating of Alzheimer's disease, wherein said pharmaceutical agent ~~comprising~~ comprises a compound obtained by the method according to Claim 46.

Claim 52 (Currently Amended): A method for detecting Alzheimer's disease, comprising ~~the following steps of:~~

- (a) measuring the expression of a polynucleotide according to Claim 37,
- (b) comparing the measurement obtained in (a) with that obtained when the polynucleotide is expressed in healthy subjects and detecting a change in expression, and
- (c) linking Alzheimer's disease with said change in expression of the polynucleotide.

Claim 53 (Currently Amended): A method for preventing or treating Alzheimer's disease, ~~wherein the method comprises~~ comprising:

administering a pharmaceutical composition comprising as an active ingredient a compound obtained by the method according to Claim 46.

Claim 54 (Currently Amended): A polynucleotide consisting of at least 15 consecutive nucleotides of the polynucleotide of Claim 18, or consisting of at least 15 consecutive nucleotides of the full complement of the polynucleotide of Claim 18 comprising a polynucleotide according, or a nucleotide sequence complementary to the complementary strand of the polynucleotide, according to Claim 18, wherein said polynucleotide comprises at least 15 nucleotides.

Claim 55 (Withdrawn): A pharmaceutical agent comprising a compound obtained by the method according to Claim 29.

Claim 56 (Withdrawn, Currently Amended): A pharmaceutical agent for ~~prevention~~ preventing or treating of Alzheimer's disease, wherein said pharmaceutical agent ~~comprising~~ comprises a compound obtained by the method according to Claim 29.

Claim 57 (Withdrawn, Currently Amended): A pharmaceutical agent for ~~prevention~~ preventing or treating of Alzheimer's disease, wherein said pharmaceutical agent ~~comprising~~ comprises a protein according to Claim 19.

Claim 58 (Withdrawn, Currently Amended): A pharmaceutical agent for ~~prevention~~ preventing or treating of Alzheimer's disease, wherein said pharmaceutical agent ~~comprising~~ comprises a protein according to Claim 20.

Claim 59 (Withdrawn, Currently Amended): A method for preventing or treating Alzheimer's disease, ~~wherein the method comprises~~ comprising:

administering a pharmaceutical composition comprising as an active ingredient a compound obtained by the method according to Claim 29.

Claim 60 (Withdrawn, Currently Amended): A method for preventing or treating Alzheimer's disease, ~~wherein the method comprises~~ comprising:

administering a pharmaceutical composition comprising as an active ingredient the protein according to Claim 19.

Claim 61 (Withdrawn, Currently Amended): A method for preventing or treating Alzheimer's disease, ~~wherein the method comprises~~ comprising:

administering a pharmaceutical composition comprising as an active ingredient the protein according to Claim 20.

Claim 62 (Withdrawn, Currently Amended): A method for preventing or treating Alzheimer's disease, ~~wherein the method comprises~~ comprising:

administering a pharmaceutical composition comprising as an active ingredient an antisense polynucleotide complementary to the protein-coding sequence of a polynucleotide according to Claim 18.

Claim 63 (Withdrawn): A pharmaceutical agent comprising a compound obtained by the method according to Claim 47.

Claim 64 (Withdrawn, Currently Amended): A pharmaceutical agent for ~~prevention~~ preventing or treating of Alzheimer's disease, wherein said pharmaceutical agent comprising a compound obtained by the method according to Claim 47.

Claim 65 (Withdrawn, Currently Amended): A pharmaceutical agent for ~~prevention~~ preventing or treating of Alzheimer's disease, wherein said pharmaceutical agent comprising a peptide according to Claim 38.

Claim 66 (Withdrawn, Currently Amended): A method for preventing or treating Alzheimer's disease, ~~wherein the method comprises~~ comprising:  
administering a pharmaceutical composition comprising as an active ingredient a compound obtained by the method according to Claim 47.

Claim 67 (Withdrawn, Currently Amended): A method for preventing or treating Alzheimer's disease, ~~wherein the method comprises~~ comprising:  
administering a pharmaceutical composition comprising as an active ingredient the peptide according to Claim 38.

Claim 68 (Withdrawn, Currently Amended): A method for preventing or treating Alzheimer's disease, ~~wherein the method comprises~~ comprising:

administering a pharmaceutical composition comprising as an active ingredient an antisense polynucleotide complementary to the protein-coding sequence of a polynucleotide according to Claim 37.

Claim 69 (New): The polynucleotide according to Claim 37, which encodes a polypeptide that suppresses or promotes amyloid- $\beta$  protein aggregation.

Claim 70 (New): The polynucleotide of Claim 18 which comprises SEQ ID NO: 3, 5, 7 or 9.

Claim 71 (New): The polynucleotide of Claim 18 which encodes a protein having a amino acid sequence as set forth in SEQ ID NO: 4, 6, 8 or 10.

Claim 72 (New): The polynucleotide of Claim 18 which encodes a protein in which one or several amino acids of the amino acid sequence of SEQ ID NO: 4, 6, 8 or 10 have been substituted, deleted, inserted and/or added, wherein the overall percentage of mutations is 5% or less.

Claim 73 (New): The polynucleotide of Claim 18 which hybridizes under stringent conditions to the polynucleotide of SEQ ID NO: 3, 5, 7 or 9, wherein the stringent conditions comprise washing in 0.1 X SSC and 0.1% SDS at 65°C.

Claim 74 (New): The polynucleotide of Claim 18 which shows at least 95% identity to a nucleotide sequence as set forth in SEQ ID NO: 3, 5, 7 or 9.